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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/578,693	05/26/2000	Masaya Yamanouchi	20-4710P	9841
2292	7590	05/14/2004	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			COOK, LISA V	
			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<i>Office Action Summary</i>	Application No.	Applicant(s)
	09/578,693	YAMANOUCHI ET AL.
Examiner	Art Unit	
Lisa V. Cook	1641	

-- The MAILING DATE of this communication appars on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 22 July 2003.

2a)  This action is **FINAL**.                    2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4)  Claim(s) 2,4,6,9,16-19 and 21-24 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 2,4,6,9,16-19 and 21-24 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on 22 July 2003 is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a)  The translation of the foreign language provisional application has been received.

15)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_  
4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_  
5)  Notice of Informal Patent Application (PTO-152)  
6)  Other: \_\_\_\_\_

## DETAILED ACTION

### *Amendment Entry*

1. Applicant's response to the Office Action mailed 22 April 2003 is acknowledged (paper #19 filed 7/22/03). In amendment-D filed therein the specification was modified while claims 14-15 and 25-26 were cancelled. Currently claims 2, 4, 6, 9, 16-19, and 21-24 are currently pending and under examination.

## OBJECTIONS WITHDRAWN

### *Drawings*

2. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) or (b)(2) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed for acceptance of the photographs or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(i), three sets of drawings or photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

3. *Applicant has file a petition filed under 37 CFR 1.84(a)(2) or (b)(2) and is granted the use of colored photos as formal drawings. The formal drawing submitted 7/22/03 have been stamped approved by the Draftsperson. Accordingly the objection is withdrawn.*

## NEW GROUNDS OF REJECTION

### *Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**I.** Claims 2, 4, 6, 16, 17, 18, 22, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gorski et al. (Clinical Chemistry, 43, No.1, January 1997, pages 193-195) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290) and Simon et al. (The Journal of Biological Chemistry, 272(16) 4/18/97, 10652-10663).

Gorski et al. disclose a comparative study evaluating the increased concentration of fatty acid binding protein (FABP) concentrations in plasma samples of patients with chronic renal failure. Plasma FABP concentration was measured by a sensitive noncompetitive sandwich ELISA. PAGE 194 2<sup>nd</sup> column.

Plasma FABP concentration is shown to markedly increase in patients with chronic renal failure. Page 194, 3<sup>rd</sup> column. The findings suggest that the kidney plays a dominant role in the clearance of plasma FABP. Page 194 3<sup>rd</sup> column.

Gorski et al. differ from the instant invention in not specifically teaching the detection of liver-type fatty acid binding protein.

However, Maatman et al. identified the liver-type fatty acid binding protein utilized in the instant invention. Page 285, 1<sup>st</sup> column. This is supported by Applicants arguments (page 24 of the response filed 9/14/01 in paper #7). Maatmann et al. discloses liver-type fatty acid binding proteins and speculates that it is utilized in nephrotoxicity.

While, Simon et al. teach that the liver fatty acid binding protein functions to suppress expression in the proximal nephron (kidney). See abstract and page 10655.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the liver-type fatty acid binding protein as taught by Maatmann et al., having proven function in the kidney (nephron) as taught by Simon et al. to detect the specific kidney diseases relating to FABP in the method of Gorski et al. because Maatman et al. taught that "the liver-type FABP binds various ligands and may be involved in the renal excretion of exogenous and endogenous metabolites. The liver-type FABP also binds some drugs and may in this way prevent nephrotoxicity". Page 289, 2<sup>nd</sup> column 1<sup>st</sup> paragraph. While, Simon et al. demonstrated that the liver fatty acid binding protein [heptad repeat] mediate suppression in the stomach, liver, and kidney and represents a target for identifying transcription factors that regulate gene expression. See page 10662-1<sup>st</sup> column-last paragraph.

II. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gorski et al. (Clinical Chemistry, 43, No.1, January 1997, pages 193-195) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290) and Simon et al. (The Journal of Biological Chemistry, 272(16) 4/18/97, 10652-10663) and further in view of Kimura et al. (Journal of Biological Chemistry, 3/25/91, Vol.266., No.9., pages 5963-5972).

See discussion of Gorski et al. in view of Maatman et al. and Simon et al. as set forth above.

Gorski et al. in view of Maatman et al. and Simon et al. differ from the instant invention in failing to teach that the liver-type FABP is found in the proximal tubule of the kidney and does not cross-react with a heart muscle-type fatty acid binding protein.

However, these characteristics of  $\alpha_{2U}$ -globulin were already known in the prior art. Specifically Kimura et al. disclose that fatty acid-binding proteins found in the kidney could be distinguished according to their primary structure and histologic distribution. Two specific FABPs weighing 14 and 15.5 kDa were found in male rat kidney cytosol. The 14 kDa compound was identified as heart FABP and localized in the cytoplasm of the epithelia of the kidney distal tubules. The 15.5 kDa compound was identified as a proteolytically modified form of  $\alpha_{2U}$ -globulin (alpha 2u-globulin) and localized in the endosomes or lysosomes of kidney proximal tubules.

Gorski et al. in view of Maatman et al. and Simon et al. and in further view of Kimura et al. are all analogous art because they are from the same field of endeavor, both inventions teach methods involving FABP detection.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the antibody which would not cross-react with a muscle-type fatty acid binding protein as taught by Kimura et al., to detect the specific kidney FABP in the method of Gorski et al. in view of Maatman et al. and Simon et al. because such antibodies as taught by Kimura et al. are well known in the art.

A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such antibody assays, because Kimura et al. had already taught that the kidney contained two different types of fatty acid binding proteins, one designated the heart-FABP and the other designated the kidney-FABP. (page 5964, Results).

One having ordinary skill in the art would have been motivated to distinguish between the two types by employing an antibody that would not cross react with the other type (heart-FABP/kidney distal tubules) in order to receive an accurate, more precise measure of the concentration of the FABP of interest (in this case kidney-FABP/ kidney proximal tubules).

**III.** Claims 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gorski et al. (Clinical Chemistry, 43, No. 1, January 1997, pages 193-195) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290) and Simon et al. (The Journal of Biological Chemistry, 272(16) 4/18/97, 10652-10663) and further in view of Galaske et al. (Pflugers Archives European Journal of Physiology, 1978, 375,3, 269-277-ABSTRACT ONLY).

Please see previous discussions of Gorski et al. in view of Maatman et al. and Simon et al.

Gorski et al. in view of Maatman et al. and Simon et al. differ from the instant invention in not teaching a detection system involving a chronic renal disease (anti-GMB-nephritis model) further monitoring specimen collection at various intervals.

Galaske et al. disclosed the glomerular filtration and tubular uptake of plasma proteins in the acute heterologus phase of an anti-GMB nephritis model. Injections of anti-glomerular-basement membrane serum (anti-GMB-serum) were evaluated in tubular reabsorption and tubular flow at various times. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a anti-GMB nephritis model as taught by Galaske et al., to detect kidney diseases via proteins in the method of Gorski et al. in view of Maatman et al. and Simon et al. because Galaske et al. disclose that such models existed allowing for protein detection in plasma and urine.

One of ordinary skill in the art would have been motivated to do this in order to detect renal disorders at the onset and follow the disease progression/regression.

**IV.** Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gorski et al. (Clinical Chemistry, 43, No.1, January 1997, pages 193-195) in view of Maatman et al. (Biochem. J. 1992, 288, pages 285-290) and Simon et al. (The Journal of Biological Chemistry, 272(16) 4/18/97, 10652-10663) and further in view of Zuk et al. (U.S. Patent #4,281,061).

The teachings of over Gorski et al. in view of Maatman et al. and Simon et al. are set forth above. Although the reference teaches reagents for examining kidney disease, the references fail to teach the assay as a kit.

However, Zuk et al. (4,281,061) teach that “as a matter of convenience the reagents [of an immunoassay] can be provided as kits, where the reagents are in predetermined ratios, so as to substantially optimize the sensitivity of the assay in the range of interest” (column 22, lines 63-66).

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant’s invention to take the kidney disease detection assay as taught by over Gorski et al. in view of Maatman et al. and Simon et al. and format them into a kit because Zuk et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay.

### ***Response to Arguments***

5. Applicant contends that the primary references do not teach the instant invention for the following reasons:

Gorski et al. is focused on heart-type FABP as a marker for myocardial infarction, further teaching away from the instant invention because heart type FABP and liver-type FABP are different structures. This argument was carefully considered but not found persuasive because Gorski et al. is cited in combination with two other references, which must be considered in combination. Although Gorski et al. do not specifically detect liver-type FABP the structure is taught to be relevant in kidney disorders in the references of Maatman et al. and Simon et al.

Gorski et al. further teaches not only myocardial infarction but is also concerned with chronic renal failure. This is supported on page 194, 1<sup>st</sup> paragraph "we studied plasma FABP and myoglobin in patients with chronic renal failure" and page 194 3<sup>rd</sup> paragraph "The present data are the first to show plasma FABP concentration is markedly increased in patients with chronic renal failure and normal heart function, similar to that found for myoglobin." "These findings suggest that the kidney plays a more dominant role in the clearance of plasma FABP than of myoglobin."

With respect to Maatman et al. applicant contends that the reference is drawn to both L-FABP and H-FABP and although disclosing that L-FABP may prevent nephotoxicity (be involved in kidney disease), this is mere speculation. This argument was carefully considered and the rejection was modified to include Simon et al. which teaches experimental analysis of liver fatty acid binding protein and it's function to suppress expression in the proximal nephron (kidney)

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

11. For reasons aforementioned, no claims are allowed.

*Remarks*

12. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Nagasawa (Japanese Med. Res. Found. Publ. 1979, 7 (Glomerulonephritis), pages 39-51)- ABSTRACT ONLY teach that the binding distribution of Con A is similar anti-nephritogenic glycoprotein antibody.

13. New grounds of rejection were presented in the Office Action. It is therefore made **NON- FINAL**. Examiner apologizes for any inconvenience this may cause Applicant.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

*Lisa Cook*

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